REMARKS

This is in response to the Office Action that was mailed on March 12, 2002. Claims 1, 2, 6, and 17 have been amended without change in scope and without the introduction of new matter. Regarding claim 6, the former definitions of R_{6a} and Q', which had incorporated definitions from other locations, have been made explicit – based upon the definitions in claim 19 – in order to enhance the readability of claim 6. Claims 1, 2, 5-9, 11, 16-19 are in the case.

The claims were rejected under the second paragraph of 35 USC 112 as failing to define the invention properly. The term "comprising" in the definition of heteroaryl has been replaced by more explicit language, and the definition of "cyclic amino group" has been amended to make it clear that it does not include groups which are not encompassed by its terms. The claims in their present form satisfy the requirements of the statute.

It is noted that the Examiner has cited, but not applied, WO 99/40075.

The Examiner is respectfully requested to pass this application to issue. Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Richard Gallagher (Reg. No. 28,781) at (703) 205-8008, in order to conduct an interview in an effort to expedite the prosecution of the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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By _____
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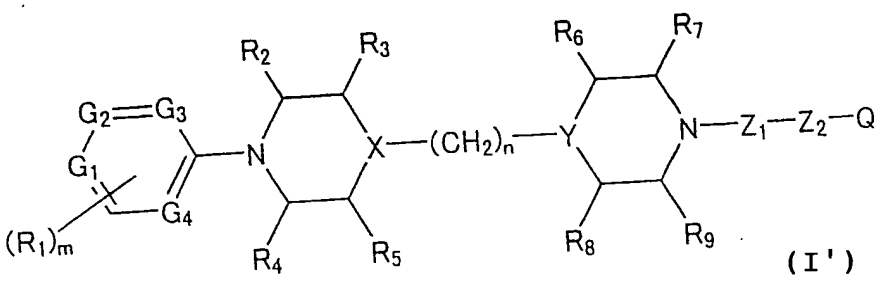
Attachment: Version with Markings to Show Changes Made

VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (twice amended) A method for treating a disease for which the FXa inhibitor is indicated, comprising: administering an effective amount of a composition comprising a pharmaceutical carrier and at least one compound represented by the following formula (I') or a salt thereof:



(I')

[(]wherein G_1, G_2, and G_3 are independently CH or N and G_4 is CH, provided that one or two of G_1 to G_3 is N;

X is CH and Y is N;

Z_1 is a group represented by the formula $-SO_2-$ or $-CH_2-$;

Z_2 is a single bond, a lower alkylene group, a lower alkenylene group or a lower alkynylene group;

Q is an optionally substituted aryl group in the form of a monocyclic or fused hydrocarbon ring having 6-14 carbon atoms or an optionally substituted heteroaryl group in a monocyclic or fused cyclic form having 1-4 heteroatoms selected from the group consisting of oxygen, sulfur, and nitrogen atoms [comprising an oxygen, a sulfur, or a nitrogen atom];

R_1 is either any substituent selected from group A (a hydrogen atom;[,] a halogen atom;[,] a trifluoromethyl group;[,] a trifluoromethoxy group;[,] a carboxyl group;[,] a carbamoyl group;[,] an amino group;[,] a cyano group;[,] a nitro group;[,] a lower alkanoyl group;[,] a lower alkoxy group;[,] a lower alkoxycarbonyl group;[,] a mono- or di-substituted lower alkylamino group;[,] a cyclic amino group optionally substituted by a lower alkyl group or a hydroxyl group and being a pyrrolidinyl group, a piperidinyl group, a morpholino group, or a piperazinyl

group;[,] a lower alkanoylamino group;[,] a phenyl group;[,] a phenoxy group;[,] a benzyloxy group;[,] a benzoyl group;[,] a mercapto group;[,] a lower alkylthio group;[,] a lower alkylthiocarbonyl group;[,] a hydroxyl group; or a mono- or di-substituted lower alkylaminocarbonyl group), or an oxygen atom that forms a N-oxide group with N in any one of G1 – G4, or a lower alkyl group or a lower alkenyl group that may be substituted with a desired number of substituents of group A or a lower alkoxy group or a lower alkoxy group which may be substituted with a desired number of substituents of group A or a lower alkoxy group;

each of R_2, R_3, R_4, R_5, R_6, R_7, R_8 and R_9 forms an oxo group when combined with the carbon atom on the ring to which they are bound, or they are each a hydrogen atom, a carboxyl group, a lower alkylcarbonyl group, a lower alkoxycarbonyl group, a lower alkoxycarbonylalkylcarbonyl group, an optionally mono- or di-lower alkyl substituted carbamoyl group, a lower alkoxycarbamoyl group, a lower alkoxycarbonylalkylcarbamoyl group, a pyrrolidin-1-ylcarbonyl group, a morpholinocarbonyl group, a piperazin-1-ylcarbonyl group that may be substituted by a methyl group in 4-position, a piperidin-1-ylcarbonyl group that may be substituted by a methyl group or a hydroxyl group in 4-position, an N-phenylcarbamoyl group or a group represented by the formula $-CONH(CH_2)_pS(O)_qR_{10}$ or $-CONH(CH_2)_rNR_{11}R_{12}$, or a lower alkyl group that may be substituted by R_{15};

each of R_{10}, R_{11} and R_{12} independently represents a hydrogen atom, a lower alkyl group, a phenyl group or a lower alkylphenyl group;

R_{15} is a carboxyl group, a lower alkoxycarbonyl group, a hydroxyl group, a lower alkoxy group, a lower alkanoyloxy group, an amino group, a mono- or di-substituted lower alkylamino group, a lower alkanoylamino group, a lower alkylsulfonylamino group, a cyclic amino group optionally substituted by a lower alkyl group or a hydroxyl group and being a pyrrolidinyl group, a piperidinyl group, a morpholino group, or a piperazinyl group, or an N-hydroxyimino group;

provided that R_6 may also represent two lower alkyl groups in geminal;

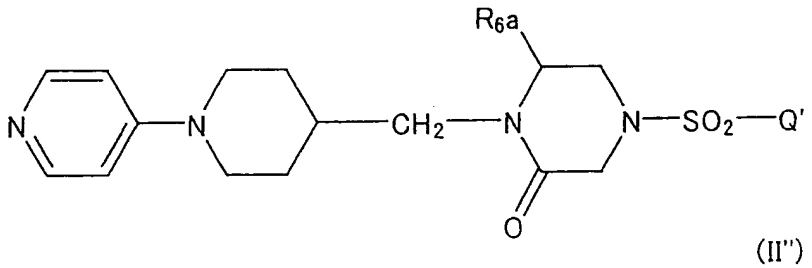
also provided that if any one of the substituents R_2 - R_9 includes cyclic group, such cyclic group may be substituted by one or two lower alkyl groups;

m is an integer of 0 - 3 and n is 1, p is an integer of 0 - 4, q is an integer of 0 - 2, and r is an integer of 1 – 4.

2. (thrice amended) The method according to claim 1, wherein the substituent of the optionally substituted aryl or heteroaryl group as Q of the formula (I') is 1 - 4 groups in any combinations that are selected from among substituents of either group B (a halogen atom, a trifluoromethyl group, a trifluoromethoxy group, a trifluoromethanesulfonyl group, a carboxyl group, a carbamoyl group, an amino group, a cyano group, a nitro group, a lower alkanoyl group, a lower alkoxyl group, a lower alkoxycarbonyl group, a mono- or di-substituted lower alkylamino group, a lower alkanoylamino group, a cyclic amino group optionally substituted by a lower alkyl group or a hydroxyl group and being a pyrrolidinyl group, a piperidinyl group, a morpholino group, or a piperazinyl group, a mercapto group,, a lower alkylthio group, a lower alkylthiocarbonyl group, a lower alkylsulfonyl group, a lower alkylsulfinyl group, a hydroxyl group or a mono- or di-substituted lower alkylaminocarbonyl group, an amidino group which is optionally substituted with sulfamoyl or carbamoyl group, the formula $-NHCR_{13}-NHR_{14}$ (wherein R_{13} is an optionally cyano-substituted imino group or a group $-CHNO_2$; R_{14} is a hydrogen atom or a methyl group), a phenyl group, a phenoxy group, a heteroaryl group, a heteroaryloxy group, or a group represented by phenyl-S(0)t or heteroaryl-S(0)t (wherein t is an integer of 0 – 2), the heteroaryl group of group B is a 5- or 6-membered aromatic monocyclic group containing not more than four oxygen atoms, sulfur atoms or nitrogen atoms, provided that all aromatic rings of group B may be mono-, di-, or tri-substituted by any substituent of group C (a halogen atom, a trifluoromethyl group, a cyano group, a hydroxyl group, an amino group, a mono- or di-substituted lower alkylamino group, a cyclic amino group optionally substituted by a lower alkyl group or a hydroxyl group and being a pyrrolidinyl group, a piperidinyl group, a morpholino group, or a

piperazinyl group, a nitro group, a carboxyl group, a mono or di-substituted lower alkylaminocarbonyl group, a lower alkyl group, a lower alkoxy group or a lower alkoxycarbonyl group)) or a lower alkyl group that may be substituted by a desired number of substituents of group B.

6. (amended) A compound of the formula (II"):



(II")

[(wherein R_{6a} and Q' have the same definitions as given for the substituent R_{6a} but not a hydrogen and Q' in the formula (II'))]

wherein

R_{6a} is

1) a group selected from among a carboxyl group, a lower alkylcarbonyl group, a lower alkoxycarbonyl group, and a lower alkoxycarbonylalkylcarbonyl group;

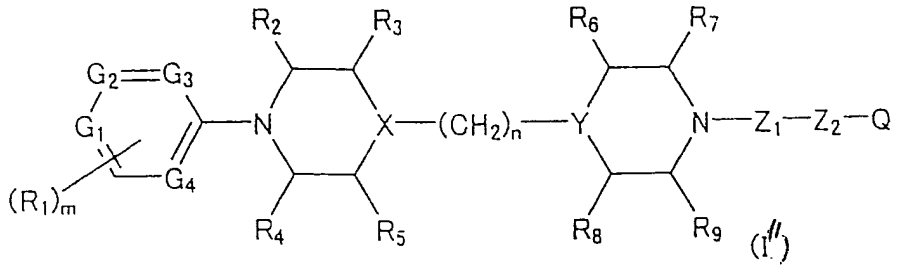
2) a group selected from among an optionally mono- or di-lower alkyl substituted carbamoyl group, a lower alkoxycarbamoyl group, a lower alkoxycarbonylalkylcarbamoyl group, a pyrrolidin-1-ylcarbonyl group, a morpholinocarbonyl group, a piperidin-1-ylcarbonyl group which may be substituted by a methyl group or a hydroxyl group in 4-position, an N-phenylcarbamoyl group or a group selected from among the groups represented by the formulae $-CONH(CH_2)_pS(O)_qR_{10}$ and $-CONH(CH_2)_rNR_{11}R_{12}$ (wherein R_{10}, R_{11}, and R_{12} are independently a hydrogen atom, a lower alkyl group, a phenyl group, or a lower alkylphenyl group; p is an integer of 0-4, q is an integer of 0-2, and r is an integer of 1-4), or

3) a lower alkyl group optionally substituted by R_{15}; R_{15} is a carboxyl group, a lower alkoxycarbonyl group, a hydroxyl group, a lower alkoxy group, a lower alkanoyloxy group, an amino group, a mono- or di-substituted lower alkylamino group, a lower alkanoylamino group, a lower alkylsulfonylamino group, a cyclic amino group optionally substituted by a lower alkyl group or a hydroxyl group and being a pyrrolidinyl group, a piperidinyl group, a morpholino group, or a piperazinyl group, or an N-hydroxyimino group; and

Q' represents $-Z_2-Q$, wherein Z_2 is a single bond, a lower alkylene group, a lower alkenylene group, or a lower alkynylene group and Q is an optionally substituted aryl group in the form of a monocyclic or fused hydrocarbon ring having 6-14 carbon atoms or an optionally substituted heteroaryl group in a monocyclic or fused cyclic form having 1-4 heteroatoms comprising an oxygen, a sulfur, or a nitrogen atom

or a salt thereof.

17. (twice amended) A compound represented by the following formula (I") or a salt thereof:



(I")

[(]wherein G_1, G_2, and G_3 are independently CH or N and G_4 is CH, provided that one or two of G_1 to G_3 is N;

X is CH and Y is N;

Z_1 is a group represented by the formula $-SO_2-$ or $-CH_2-$;

Z_2 is a single bond, a lower alkylene group, a lower alkenylene group or a lower alkynylene group;

Q is an optionally substituted aryl group in the form of a monocyclic or fused hydrocarbon ring having 6-14 carbon atoms or an optionally substituted heteroaryl group in a monocyclic or fused cyclic form having 1-4 heteroatoms selected from the group consisting of oxygen, sulfur, and nitrogen atoms [comprising an oxygen, a sulfur, or a nitrogen atom];

R_1 is either any substituent selected from group A (a hydrogen atom[,] a halogen atom[,] a trifluoromethyl group[,] a trifluoromethoxy group[,] a carboxyl group[,] a carbamoyl group[,] an amino group[,] a cyano group[,] a nitro group[,] a lower alkanoyl group[,] a lower alkoxy group[,] a lower alkoxycarbonyl group[,] a mono- or di-substituted lower alkylamino group[,] a cyclic amino group optionally substituted by a lower alkyl group or a hydroxyl group and being a pyrrolidinyl group, a piperidinyl group, a morpholino group, or a piperazinyl group[,] a lower alkanoylamino group[,] a phenyl group[,] a phenoxy group[,] a benzyloxy group[,] a benzoyl group[,] a mercapto group[,] a lower alkylthio group[,] a lower alkylthiocarbonyl group[,] a hydroxyl group; or a mono- or di-substituted lower alkylaminocarbonyl group), or an oxygen atom that forms a N-oxide group with N in any one of G1 – G4, or a lower alkyl group or a lower alkenyl group that may be substituted with a desired number of substituents of group A or a lower alkoxy group or a lower alkoxy group which may be substituted with a desired number of substituents of group A or a lower alkoxy group;

each of R_2, R_3, R_4, R_5, R_6, R_7, R_8 and R_9 forms an oxo group when combined with the carbon atom on the ring to which they are bound, or they are each a hydrogen atom, a carboxyl group, a lower alkylcarbonyl group, a lower alkoxycarbonyl group, a lower alkoxycarbonylalkylcarbonyl group, an optionally mono- or di-lower alkyl substituted carbamoyl group, a lower alkoxycarbamoyl group, a lower alkoxycarbonylalkylcarbamoyl group, a pyrrolidin-1-ylcarbonyl group, a morpholinocarbonyl group, a piperazin-1-ylcarbonyl group that may be substituted by a methyl group in 4-position, a piperidin-1-ylcarbonyl group that may be substituted by a methyl group or a hydroxyl group in 4-position, an N-phenylcarbamoyl group or a group represented by the formula -

$CONH(CH_2)_pS(O)_qR_{10}$ or $-CONH(CH_2)_rNR_{11}R_{12}$, or a lower alkyl group that may be substituted by R_{15};

each of R_{10}, R_{11} and R_{12} independently represents a hydrogen atom, a lower alkyl group, a phenyl group or a lower alkylphenyl group;

R_{15} is a carboxyl group, a lower alkoxycarbonyl group, a hydroxyl group, a lower alkoxy group, a lower alkanoyloxy group, an amino group, a mono- or di-substituted lower alkylamino group, a lower alkanoylamino group, a lower alkylsulfonylamino group, a cyclic amino group optionally substituted by a lower alkyl group or a hydroxyl group and being a pyrrolidinyl group, a piperidinyl group, a morpholino group, or a piperazinyl group, or an N-hydroxyimino group;

provided that R_6 may also represent two lower alkyl groups in geminal;

also provided that if any one of the substituents R_2 - R_9 includes cyclic group, such cyclic group may be substituted by one or two lower alkyl groups; m is an integer of 0 - 3 and n is 1, p is an integer of 0 - 4, q is an integer of 0 - 2, and r is an integer of 1 – 4;

with the proviso that when these compounds of formula (I") in which all of R_2, R_3, R_4, R_5, R_6, R_7, R_8 and R_9 are independently selected from hydrogens or oxo groups and Q is selected from the group consisting of five- or six-membered heterocycle, phenyl, phenyl alkenyl, and naphthyl, any of which is optionally substituted, are excluded.